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1 disclosed by Bard. Applicants have amended independent Claim 1 and added new Claim 37 to more  
2 clearly highlight these distinguishing elements.

3 With respect to Claim 1, it is clear that Bard's controller can be used to control elements  
4 included in Bard's reaction system, including pumps, valves and a thermal conditioning system.  
5 Bard's controller is also logically coupled to one or more detectors. Bard clearly indicates that the  
6 controller can be used to optimize control of residence time within a reaction zone (Abstract). The  
7 Examiner notes that Bard discloses that his reaction system can be monitored to regulate the reaction  
8 process and/or create an optimal environment for synthesis. Clearly, one can program Bard's  
9 controller with a set of optimal reaction conditions, and Bard's controller will monitor the reaction  
10 system to ensure that those optimal reaction conditions are met. Significantly, Bard's controller is  
11 configured to address a different need than the controller in applicants' invention is configured to  
12 meet. Specifically, Bard's controller is used to control the functioning of a reaction system according  
13 to optimal reaction parameters that are programmed into the control system. Applicants' controller is  
14 configured to perform a plurality of optimization experiments in order to determine those optimal  
15 reaction parameters. As amended, Claim 1 specifically recites that the controller is configured to  
16 implement a plurality of optimization experiments, *"wherein during each of the plurality of*  
17 *optimization experiments, at least one of a plurality of reaction parameters controlled by the*  
18 *controller is changed, the plurality of reaction parameters including at least the parameters of*  
19 *temperature and reactant concentration."* As discussed in detail in applicants' specification, the  
20 controller in the present invention is configured to selectively vary a set of reaction parameters  
21 according to a predefined protocol, and to collect data corresponding to the chemical products  
22 produced under those reaction parameters. By comparing the data collected from the plurality of  
23 different optimization experiments, a set of optimal reaction parameters can be identified. Those  
24 optimal reaction parameters can then be used in Bard's reaction system to produce a chemical product  
25 under optimal conditions.

26 *Argeundo*, from a structural standpoint Bard's controller *could* be configured to continuously  
27 implement a plurality of different optimization experiments, to selectively vary a set of reaction  
28 parameters according to a predefined protocol, and to collect data corresponding to the chemical  
29 products produced under those reaction parameters. However, Bard does not teach or suggest  
30 programming or otherwise configuring a controller to implement those specific functions. Thus

1 applicants' recited controller can be structurally distinguished over the controller described by Bard,  
2 on the basis of the functions the controller is configured to implement. As noted in applicants'  
3 *Background of the Invention* section, prior art systems configured to determine optimal reaction  
4 parameters generally perform optimization experiments as a batch process, as opposed to a  
5 continuous process, or perform optimization experiments using a chemical reaction system  
6 configured to simultaneously execute a series of parallel reactions, in which a different reaction  
7 parameter is varied in each of the parallel reactions. Significantly, there is no evidence to indicate  
8 that one of ordinary skill in the art would have recognized that Bard's reaction system could be  
9 modified/programmed to implement a series of optimization experiments to identify optimal reaction  
10 parameters in a continuously running system. The cited art simply does not teach or suggest such a  
11 modification, nor is there any evidence that such a modification would solve the problem recognized  
12 in the art.

13 Thus Claim 1 as amended distinguishes over Bard, and each claim depending on Claim 1 is  
14 distinguished over Bard for at least the same reasons. Accordingly, the rejection of Claims 1-8 as  
15 being anticipated by Bard should be withdrawn."

16 Claim 5 has been amended to further recite that the predefined protocol implemented by the  
17 processor to carry out the plurality of optimization reactions comprises at least one of:  
18 *"implementing a plurality of optimization experiments in which each reaction parameter has been*  
19 *predefined; implementing a plurality of optimization experiments in which each reaction parameter*  
20 *is varied between a predefined maximum value and a predefined minimum value based on a*  
21 *predefined function; and implementing a plurality of optimization experiments in which each reaction*  
22 *parameter in an initial set of optimization experiments are predefined, and in which at least one*  
23 *reaction parameter in a later set of optimization experiments is determined based on results from the*  
24 *initial set of optimization experiments."* Bard does not teach or suggest any equivalent predefined  
25 protocol for implementing a plurality of optimization reactions. Claim 5 is therefore distinguishable  
26 over Bard for this additional reason,

27 The Examiner has also rejected claims in the present application based on Dasgupta, as will  
28 be discussed in greater detail below. Even if one of ordinary skill in the art would have been  
29 motivated to modify Bard's controller based on Dasgupta's disclosure, an equivalent invention would  
30 not be achieved. Significantly, Dasgupta does not teach or suggest a controller configured to control

1 a reactor system to produce a chemical product. Dasgupta specifically refers to controlling an  
2 *analytical technique* referred to as titration. Dasgupta teaches a controller configured to control the  
3 titration process by manipulating the relative concentrations of a sample and a titrant so that the total  
4 flow in the system is constant (that is, when the flow of the titrant is increased, the flow of sample is  
5 decreased, see paragraph 14 of Dasgupta). Thus, Dasgupta teaches controlling an analytical  
6 technique using a controller configured to continuously control the concentrations and flow rates of  
7 both a sample and a titrant. Note that Claim 1 specifically recites a controller configured to control  
8 reaction parameters including *at least* temperature and reactant concentration. At best, modifying  
9 Bard's controller in view of Dasgupta would achieve a controller configured to selectively vary  
10 reactant concentrations over time. The cited art does not teach or suggest configuring a controller to  
11 selectively vary a plurality of reaction parameters while continuously performing a plurality of  
12 optimization experiments, where the plurality of reaction parameters include both temperature and  
13 reactant concentration.

14 Furthermore, it must be recognized that Dasgupta does not teach a controller configured to  
15 control a chemical reactor. Dasgupta is not directed to the generation of a chemical product, and  
16 there is no reason to conclude that one of ordinary skill in the art would have looked to a technique  
17 for controlling an analytical process for guidance in modifying a controller to control a system and  
18 process involved in generating a chemical product. Dasgupta **does not** teach or suggest techniques  
19 directed to determining optimal reaction parameters for a reaction; instead, Dasgupta teaches a  
20 controller configured to control a continuous chemical analytical process involving a sample and a  
21 titrant. Thus, there does not appear to be any motivation to combine the references in the manner  
22 suggested by the Examiner, and such a combination does not support a *prima facie* basis for rejecting  
23 applicants' claims as obvious.

24 Applicants further respectfully submit that Claims 4, 7, and 8 were distinguishable over Bard  
25 even before the above-noted amendment to Claim 1. Claim 4 specifically recites a controller  
26 configured to implement a particular function involving directing a flow of fluid through a plurality  
27 of residence time chambers. Merely because Bard discloses a chemical reactor that can be used in  
28 connection with a residence time chamber (or a plurality of residence time chambers) does not merit  
29 a conclusion that Bard discloses a controller that implements a function equivalent to that claimed by  
30 applicants. FIGURES 1B-1E as filed with the present application schematically illustrate the control

1 function recited in Claim 4. Significantly, neither Bard nor Dasgupta teaches or suggests an  
2 equivalent control function. Claim 4 is therefore distinguishable over the cited art for this additional  
3 reason.

4 Claims 7 and 8 specifically recite a controller configured to selectively control a specific  
5 reaction parameter over time while monitoring the chemical product produced using those reaction  
6 parameters, in order to determine optimal reaction parameters. Bard's system is configured to  
7 receive input from a user, so that once optimal reaction parameters have been determined, Bard's  
8 invention implements the optimal reaction parameters and controls the reaction system to adhere to  
9 these previously determined optimal reaction parameters. Neither Bard nor Dasgupta teaches or  
10 suggests a controller configured to perform a plurality of optimization experiments by selectively  
11 varying the reaction parameters while collecting analytical data about the product produced using  
12 those reaction parameters to determine optimal reaction parameters.

13 Rejection under 35 U.S.C. § 103

14 The Examiner has also rejected Claims 9-13 under 35 USC § 103(a) as being unpatentable  
15 over Bard (U.S. 5,580,523) in view of Dasgupta (U.S. Patent Publication 20020151080). The  
16 Examiner asserts that Dasgupta discloses monitoring reaction parameters according to a periodic  
17 pattern and asserts that it would have been obvious to one of ordinary skill in the art at the time of the  
18 invention to have modified Bard's controller using Dasgupta's control techniques for optimizing  
19 continuously monitored parameters of an automated reaction system. Applicants respectfully  
20 disagree for the following reasons.

21 With respect to Bard, the Examiner appears to have concluded that Bard discloses a reaction  
22 system configured to determine optimal reaction parameters. Applicants respectfully submit that  
23 Bard does not teach or suggest any control techniques that can be used to *determine* optimal reaction  
24 parameters. Instead, Bard discloses a reaction system and a controller configured to *maintain*  
25 optimal reaction conditions. Clearly, those optimal reaction parameters must be provided to Bard's  
26 controller in order for Bard's reaction system to function. Bard does not teach or suggest a technique  
27 for actually *determining* those optimal reaction parameters. Significantly, Dasgupta also does not  
28 teach or suggest a technique for determining optimal reaction parameters. Accordingly, it is not  
29 apparent how a combination of these two references could achieve applicants' claimed invention,  
30 which as recited in Claim 1 (as amended), is directed to a system including a controller configured to

1 continuously perform "a plurality of optimization experiments, such that during each of the plurality  
2 of optimization experiments, at least one of a plurality of reaction parameters controlled by the  
3 controller is changed according to a predefined protocol, the plurality of reaction parameters  
4 including at least the parameters of temperature and reactant concentration, the plurality of  
5 optimization experiments enabling optimal reaction parameters to be identified."

6 Dasgupta teaches a technique for controlling an analytical process (titration) by selectively  
7 varying the flow of a titrant, while ensuring that the flow of the sample is simultaneously controlled  
8 to achieve a total constant flow (in particular, see paragraphs 14 and 31 of Dasgupta). It is not  
9 apparent why one of ordinary skill in the art would consider a control technique configured to control  
10 titration would be applicable to controlling a plurality of optimization experiments conducted in order  
11 to determine optimal reaction parameters to be implemented in producing a desired chemical product.  
12 Significantly, Dasgupta does not teach or suggest that the control techniques disclosed therein would  
13 have any applicability to controlling a system configured to produce a chemical product, as opposed  
14 to controlling a system configured to implement titration based analysis. There is no basis to  
15 conclude that the problems encountered in titration analysis have any relationship to the problems  
16 encountered in controlling a chemical reaction. There is no basis in the cited art for concluding that  
17 one of ordinary skill in the art at the time of the invention would have been led to modify Bard's  
18 controller in view of Dasgupta's disclosure. Thus, as discussed above, the suggested combination of  
19 Bard and Dasgupta does not support a *prima facie* for rejecting applicants' claims as obvious.

20 It should also be noted that in suggesting the combination of Bard and Dasgupta as supporting  
21 a rejection of applicants' claims, the Examiner has not indicated any expected benefit that would  
22 motivate one of ordinary skill in the art to make such a combination. A proper obviousness rejection  
23 must include an identification of the motivation that would lead one of ordinary skill in the art to  
24 make such combination, and that motivation does not appear to be present with respect to a proposed  
25 combination of Bard and Dasgupta.

26 Furthermore, even if Bard's controller were modified in view of Dasgupta, the resulting  
27 controller would only be configured to vary the concentrations of the reactants such that the total  
28 flow remains the same. As noted above, Claim 1 has been amended to specifically recite that the  
29 reaction parameters varied by the controller include *temperature and concentration*. While Bard's  
30 controller is configured to enable temperature control, there is no teaching in Bard or in Dasgupta of

1 a control technique that continuously selectively varies at least one of a plurality of parameters that  
2 includes temperature and concentration. Thus, the combination of references suggested by the  
3 Examiner does not achieve an equivalent invention. Claim 1 as amended distinguishes over the  
4 combination of Bard and Dasgupta, and each claim depending on Claim 1 is distinguished over the  
5 cited art for at least the same reasons. Accordingly, the rejection of Claim 1-13 as being obvious  
6 over Bard in view of Dasgupta should be withdrawn.

7 Claim 12 specifically recites that each of at least two reaction parameters *are varied by the*  
8 *controller according to different periodic functions*. Dasgupta teaches that while a preferred  
9 embodiment implements a linear scan rate to selectively vary the flow rate of the titrant, different  
10 scan rates, having different waveforms (including waveforms with increasing and decreasing slopes),  
11 can be employed to control the flow rate of the titrant (see paragraph 54). However, using different  
12 functions to selectively vary the flow rate of the titrant is not equivalent to varying at least two  
13 reaction parameters using different periodic functions. According to Dasgupta, both the flow rate of  
14 the titrant and the flow rate of the sample are controlled based on a single function. Whatever  
15 function is used to vary the flow rate of the titrant must also be used to determine the change in the  
16 flow rate of the sample, because as disclosed by Dasgupta, any change in the flow rate of the titrant  
17 must also result in a corresponding change in the flow rate of the sample, so that a constant flow rate  
18 is maintained (see paragraph 14). The control scheme of Dasgupta is thus not equivalent to varying  
19 at least two reaction parameters according to different periodic functions, as claimed by applicants.  
20 Claim 12 is distinguishable over the combination of Bard and Dasgupta for this additional reason.

21 Claim 13 also includes subject matter that goes beyond any possible combination of Bard and  
22 Dasgupta. Claim 13 specifically recites that after at least two reaction parameters have been varied  
23 according to their respective functions, the controller is configured to identify new upper and lower  
24 boundaries for those reaction parameters. The controller then redefines the periodic functions, and  
25 once again selectively varies the reaction parameters based on those redefined periodic functions.  
26 Dasgupta does not teach or suggest identifying new upper and lower boundaries for each reaction  
27 parameter and redefining the periodic function used to selectively vary that reaction parameter.  
28 Claim 13 is distinguishable over the combination of Bard and Dasgupta for this additional reason.  
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1 Patentability of Newly Added Claims

2 New Claims 35-38 have been added in the present amendment. These claims are fully  
3 supported by the specification and are consistent with the election made in response to the restriction  
4 requirement.

5 Claim 35 depends from Claim 1, and is therefore patentable for at least the same reason as  
6 Claim 1. Furthermore, Claim 35 recites that the controller is configured to use a baseline value for  
7 each reaction parameter to generate the desired product, then determine at least one of a quantity and  
8 a quality of the desired product generated using the baseline values, change the baseline value for at  
9 least one reaction parameter, thereby affecting the desired product being produced by the automated  
10 system, and then determine at least one of a quantity and a quality of the desired product generated  
11 using the at least one baseline value that was changed. As discussed above, Bard does not teach or  
12 suggest *any* technique that can be used to determine optimal reaction parameters. Dasgupta teaches  
13 controlling an analytical technique using one of a plurality of different functions to selectively vary  
14 the flow rate of the titrant and a sample. Significantly, Dasgupta does not teach or suggest a control  
15 technique that first employs a baseline value and then modifies the baseline value based on data  
16 obtained in conjunction with the baseline value. Such a technique recited by applicants' claim is  
17 distinctly different than varying a flow rate of the titrant and sample based on a predefined function,  
18 as is done by Dasgupta. Thus, Claim 35 is distinguishable over the combination of Bard and  
19 Dasgupta for this additional reason.

20 Claim 36 also depends from Claim 1, and also is therefore patentable for at least the same  
21 reason as Claim 1. Claim 36 recites that the controller is configured to use a baseline value for each  
22 reaction parameter to generate the desired product, to selectively vary each baseline value based on a  
23 linear function, and whenever a linear discontinuity is identified, to redefine the baseline value.  
24 Neither Bard nor Dasgupta teach or suggest a control technique including the function of redefining a  
25 baseline value whenever a linear discontinuity is identified. Thus, Claim 36 is distinguishable over  
26 the combination of Bard and Dasgupta for this additional reason.

27 Claim 37 is based on Claim 1 (before it was amended), and incorporates additional language  
28 further defining the dilution pumps. Specifically, Claim 37 recites a reaction system configured to  
29 produce the desired chemical product using at least two different reactants, and which includes a  
30 dilution pump for each reactant. The dilution pumps are configured to be coupled in fluid



1 communication with a corresponding reactant supply source and with the solvent supply source for a  
2 corresponding reactant, and to be logically coupled to the controller. Significantly, the dilution  
3 pumps are *operative to vary a concentration of a corresponding reactant using a solvent, such that*  
4 *the concentration of each reactant can be varied independently of the concentration of each other*  
5 *reactant*. Bard discloses a reaction system that includes two reactant supplies and a solvent supply.  
6 Bard specifically teaches that the solvent supply is not used to dilute either reactant. Instead, the  
7 solvent supply is used to flush the system and between different reactions. Even if one were to use  
8 the solvent supply disclosed by Bard to change the concentration of a reactant, because of the  
9 structural configuration disclosed by Bard, the solvent supply can only be used to vary the  
10 concentration of both reactants simultaneously. Bard's solvent supply is coupled in fluid  
11 communication with the mixing volume, and each reactant supply is also coupled in fluid  
12 communication with the mixing volume. If the solvent pump is not activated, then only the two  
13 reactants will flow into the mixing volume. If the solvent pump is activated, the solvent will also  
14 flow into the mixing volume, thereby changing the relative concentrations of each reactant by the  
15 same amount. Therefore, Bard's system is not configured to *independently* vary the concentration of  
16 each reactant using a solvent. Neither Bard, nor any other cited art, teaches or suggests that it would  
17 be desirable to modify Bard's system to enable the concentration of each reactant to be independently  
18 varied using a solvent. Dasgupta discloses that the concentration of a sample can be varied using a  
19 solvent; however, Dasgupta's titration system is not configured to vary the concentration of the titrant  
20 using a solvent (Dasgupta instead teaches changing a flow rate of the titrant using a pump). Thus, the  
21 suggested combination of Bard and Dasgupta cannot achieve an invention equivalent to applicants'  
22 claimed invention.

23 New Claim 38 recites a method for using a reaction system consistent with the elected claims  
24 to determine optimal reaction parameters. While Claim 38 may appear to be based on the non-  
25 elected claims, the Examiner had indicated that the non-elected method represent a different  
26 invention than those that have been elected, because the method originally claimed in the non-elected  
27 claims did not require the use of the dilution pumps recited in the elected claims. Claim 38 *does*  
28 include the dilution pump element recited in the elected claims, and therefore Claim 38 is consistent  
29 with the elected claims. Claim 38 distinguishes over the cited art because: (1) the combination of  
30 Bard and Dasgupta does not establish a *prima facie* case of obviousness, as discussed above; and

1 (2) Claim 38 specifically recites the step of utilizing a dilution pump to vary a concentration of each  
2 reactant by adding a solvent to the reactant. As noted above, neither Bard nor Dasgupta teaches or  
3 suggests varying the concentration of each reactant by adding a solvent to that reactant, and thus, an  
4 artisan of ordinary skill would not be motivated to modify either reference to achieve applicants'  
5 claimed invention.

6 In view of the amendments to the title and the specification, and the Remarks set forth above,  
7 it will be apparent that the claims in this application define a novel and non-obvious invention, and  
8 that the application is in condition for allowance and should be passed to issue without further delay.  
9 Should any further questions remain, the Examiner is invited to telephone applicants' attorney at the  
10 number listed below.

11 Respectfully submitted,



12  
13  
14 Michael C. King  
15 Registration No. 44,832

16 MCK/RMA:lrg

17 MAILING CERTIFICATE

18 I hereby certify that this correspondence is being deposited with the U.S. Postal Service in a sealed  
19 envelope as first class mail with postage thereon fully prepaid addressed to: Commissioner for Patents,  
Alexandria, VA 22313-1450, on April 7, 2005.

20 Date: April 7, 2005

